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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-417N]

Schedules of Controlled Substances: Placement of UR-144, XLR11, and AKB48 into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration (DEA) proposes placing (1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (UR-144), [1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144, XLR11), and *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48) including their salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible, into schedule I of the Controlled Substances Act. This proposed scheduling action is pursuant to the Controlled Substance Act which requires that such actions be made on the record after opportunity for a hearing through formal rulemaking. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, import, export, engage in research, conduct instructional activities, or possess), or propose to handle UR-144, XLR11, or AKB48.

DATES: Interested persons may file written comments on this proposal in accordance with 21 CFR 1308.43(g). Electronic comments must be submitted, and written comments must be postmarked, on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons, defined at 21 CFR 1300.01 as those “adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811),” may file a request for hearing, notice of appearance, or waiver of hearing pursuant to 21 CFR 1308.44 and in accordance with 21 CFR 1316.45, 1316.47, 1316.48, or 1316.49, as applicable. Requests for hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: To ensure proper handling of comments, please reference “Docket No. DEA-417N” on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration encourages that all comments be submitted electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the Web page or to attach a file for lengthier comments. Please go to <http://www.regulations.gov> and follow the online instructions at that site for submitting comments. Upon completion of your submission you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on Regulations.gov. If you have

received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.

- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary and are discouraged. Should you wish to mail a paper comment *in lieu of* an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/ODXL, 8701 Morrisette Drive, Springfield, Virginia 22152.

- *Hearing requests:* All requests for hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attn: Federal Register Representative/ODL, 8701 Morrisette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: Drug Enforcement Administration, Attn: Hearing Clerk/LJ, 8701 Morrisette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: John R. Scherbenske, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrisette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement Administration (DEA) for public inspection online at <http://www.regulations.gov>. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act (FOIA) applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your

comment, but do not want it to be made publicly available, you must include the phrase “PERSONAL IDENTIFYING INFORMATION” in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase “CONFIDENTIAL BUSINESS INFORMATION” in the first paragraph of your comment. You must also prominently identify confidential business information to be redacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in redacted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to <http://www.regulations.gov> may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information to this proposed rule are available at <http://www.regulations.gov> for easy reference.

Request for Hearing, Notice of Appearance at Hearing, Waiver of an Opportunity for a Hearing or to Participate in a Hearing

Pursuant to 21 U.S.C. 811(a), this action is a formal rulemaking “on the record after opportunity for a hearing.” Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551–559. 21 CFR 1308.41–1308.45; 21 CFR

part 1316, subpart D. In accordance with 21 CFR 1308.44 (a)–(c), requests for hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those “adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811).” 21 CFR 1300.01. Such requests or notices must conform to the requirements of 21 CFR 1308.44 (a) or (b), and 1316.47 or 1316.48, as applicable, and include a statement of interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver must conform to the requirements of 21 CFR 1308.44(c) and 1316.49, including a written statement regarding the interested person’s position on the matters of fact and law involved in any hearing.

Please note that pursuant to 21 U.S.C. 811(a), the purpose and subject matter of a hearing is restricted to: “find[ing] that such drug or other substance has a potential for abuse, and * * * mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of this title for the schedule in which such drug is to be placed * * *.” All requests for hearing and waivers of participation must be sent to the DEA using the address information provided above.

Legal Authority

The DEA implements and enforces Titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. 21 U.S.C. 801–971. Titles II and III are referred to as the “Controlled Substances Act” and the “Controlled Substances Import and Export Act,” respectively, and are collectively referred to as the “Controlled Substances Act” or the “CSA” for the purposes of this action. 21 U.S.C. 801–971. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR),

chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, each controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c) and the current list of scheduled substances is published at 21 CFR part 1308. 21 U.S.C. 812(a).

Pursuant to 21 U.S.C. 811(a)(1), the Attorney General may, by rule, “add to such a schedule or transfer between such schedules any drug or other substance if he * * * finds that such drug or other substance has a potential for abuse, and * * * makes with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of this title for the schedule in which such drug is to be placed * * *.” The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General (1) on her own motion; (2) at the request of the Secretary of the Department of Health and Human Services (HHS),¹ or (3) on the petition of any interested party. 21 U.S.C. 811(a). This proposed action is supported by a recommendation from the Assistant Secretary of the HHS and an evaluation of all other

¹ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary’s scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

relevant data by the DEA. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions of schedule I controlled substances on any person who handles, or proposes to handle, UR-144, XLR11, or AKB48.

Background

On April 12, 2013, the Deputy Administrator of the DEA published a Notice of Intent to temporarily place (1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (UR-144), [1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144, XLR11), and *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48) into schedule I pursuant to the temporary scheduling provisions of the CSA (78 FR 21858). On May 16, 2013, the Deputy Administrator of the DEA published a Final Order in the Federal Register (78 FR 28735) amending 21 CFR 1308.11(h) to temporarily place these three synthetic cannabinoids into schedule I of the CSA pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). That Final Order, which became effective on the date of publication, was based on findings by the Deputy Administrator of the DEA that the temporary scheduling of these three synthetic cannabinoids was necessary to avoid an imminent hazard to the public safety pursuant to 21 U.S.C. 811(h)(1). At the time the Final Order took effect, Section 201(h)(2) of the CSA (21 U.S.C. 811(h)(2)) required that the temporary scheduling of a substance expire at the end of two years from the date of issuance of the scheduling order, and it provided that, during the pendency of proceedings under 21 U.S.C. 811(a)(1) with respect to the substance, temporary scheduling of that substance could be extended for up to 1 year. Pursuant to 21 U.S.C. 811(h)(2), the temporary scheduling of UR-144, XLR11, and AKB48 expires on May 15, 2015, unless extended. An extension of the temporary order is being ordered by the DEA Administrator in a separate action.

As described in the Final Order published on May 16, 2013, UR-144, XLR11, and AKB48 are synthetic cannabinoids that are pharmacologically similar to delta 9-tetrahydrocannabinol (Δ^9 -THC) and JWH-018. While UR-144, XLR11, and AKB48 have been used as research chemicals and/or studied due to their misuse and abuse, based on the review of the scientific literature, there are no known medical uses for UR-144, XLR11, and AKB48. The Assistant Secretary of Health for the HHS has advised that there are no exemptions or approvals in effect for UR-144, XLR11, and AKB48 under section 505 (21 U.S.C. 355) of the Federal Food, Drug and Cosmetic Act (FD&C Act). As stated by the HHS, UR-144, XLR11, and AKB48 have no known accepted medical use. They are not the subject of any approved new drug applications (NDA) or investigational new drug applications (IND), and are not currently marketed as approved drug products.

Proposed Determination to Schedule UR-144, XLR11, and AKB48

Pursuant to 21 U.S.C. 811(a)(1), proceedings to add a drug or substance to those controlled under the CSA may be initiated by the Attorney General, or her delegate, the DEA Administrator. On August 31, 2013, the DEA requested a scientific and medical evaluation and scheduling recommendation from the Assistant Secretary of Health for the HHS for UR-144, XLR11, and AKB48 pursuant to 21 U.S.C. 811(b). Upon receipt of the scientific and medical evaluation and scheduling recommendations from the HHS, the DEA reviewed the documents and all other relevant data, and conducted its own eight-factor analysis of the abuse potential of UR-144, XLR11, and AKB48 pursuant to 21 U.S.C. 811(c).

Included below is a brief summary of each of the eight factors as analyzed by the HHS and the DEA, and as considered by the DEA in this proposed action. Please note that both the DEA

and the HHS analyses are available under “Supporting and Related Material” of the public docket for this proposed rule at <http://www.regulations.gov> under docket number DEA-417N.

1. *The Drug’s Actual or Relative Potential for Abuse:* As described by the HHS, the abuse potential of UR-144, XLR11, and AKB48 is associated with their ability to evoke pharmacological effects similar to those evoked by other schedule I substances that have a high potential for abuse such as Δ^9 -THC and JWH-018.

The legislative history of the CSA suggests the DEA consider the following factors when determining whether a particular drug or substance has a potential for abuse:²

- 1) There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community;
- 2) There is significant diversion of the drug or drugs containing such a substance from legitimate drug channels;
- 3) Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice; or
- 4) The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

The substances UR-144, XLR11, and AKB48 share pharmacological properties with schedule I substances, including Δ^9 -THC and JWH-018. Evaluations in animal models, specifically in drug discrimination studies, have demonstrated that cyclopropylindoles (such as UR-144 and XLR11) and indazole-3-carboximides (such as AKB48) produce Δ^9 -THC-like discriminative stimulus effects. There have also been numerous anecdotal self-reports substantiating that these substances and their products are abused by humans for their

² Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970); 1970 U.S.C.A.N. 4566, 4601.

hallucinogenic effects, as well as published reports indicating an increase in the abuse of these substances. State public health departments and poison control centers have issued warnings in response to adverse health effects associated with herbal incense products containing synthetic cannabinoids which include: tachycardia, elevated blood pressure, unconsciousness, tremors, seizures, vomiting, hallucinations, agitation, anxiety, pallor, numbness, and tingling. Numerous public health and poison control centers have issued warnings regarding the abuse of synthetic cannabinoids and their associated products. Law enforcement has also encountered incidents of exposure, primarily in response to the smoking of products purported to be laced with these substances.

2. *Scientific Evidence of the Drug's Pharmacological Effects, If Known:* As described by the HHS, UR-144, XLR11, and AKB48 have all been shown to bind to the cannabinoid 1 (CB1) receptor, act as agonists at the CB1 receptor, and substitute fully for the discriminative stimulus effects of Δ^9 -THC in the drug discrimination assay. To date, no human pharmacological studies involving UR-144, XLR11, or AKB48 have been reported.

3. *The State of Current Scientific Knowledge Regarding the Drug or Other Substance:* Synthetic cannabinoids emerged in the early 1980s. They were originally designed to investigate structure activity relationships (SAR) based on the potent substance, 9-nor-9 β -hydroxyhexahydrocannabinol (HHC). Interest in the various structural classes was generated by the mouse vas deferens (MVD) and prostaglandin synthetase activity of pravadoline and subsequent findings of affinity to the cannabinoid receptor.

The emergence of synthetic cannabinoids in the designer drug market can be traced back to the initial forensic laboratory confirmation in December 2008 at a forensic laboratory in Frankfurt, Germany that announced the identification of JWH-018 in samples of herbal incense,

and others shortly thereafter. UR-144 and XLR11 are classified as cyclopropoylindoles whereas AKB48 is classified as an indazole-3-carboximide. While UR-144 was first developed as a research tool by Abbott Laboratories, XLR11 and AKB48 were not designed for use in the laboratory and began showing up in drug seizures in 2011.

The DEA is not aware of any currently accepted medical use or NDAs for UR-144, XLR11, or AKB48. A letter dated February 14, 2013, was sent from the DEA Deputy Administrator to the Assistant Secretary for the HHS as notification of intent to temporarily place these three substances into schedule I and solicit comments, including whether there was an exemption or if an approval was in effect for the substances in question under the FD&C Act. The Assistant Secretary of HHS responded that there were no current INDs or NDAs for these synthetic cannabinoids in a letter addressed to the DEA Deputy Administrator dated March 14, 2013. In their recent scheduling recommendation, the HHS reiterated that UR-144, XLR11, and AKB48 have no known accepted medical use, are not the subject of any approved NDAs or INDs, and are not currently marketed as any approved drug products.

4. *Its History and Current Pattern of Abuse:* Synthetic cannabinoids were first reported in the United States in a December 2008 encounter, where a shipment of “Spice” was seized and analyzed by U.S. Customs and Border Protection in Dayton, Ohio. Additionally, around the same time, in December 2008, JWH-018 and cannabicyclohexanol were being identified by German forensic laboratories. Though these substances were identified in 2008, these substances likely existed and were abused some time prior to their identification.

Since the initial identification of JWH-018 in December 2008, many additional synthetic cannabinoids have been found laced on designer drug products abused for their psychoactive effects. The popularity of synthetic cannabinoids has increased tremendously since January

2010 in the United States based on seizure exhibits and media reports. This trend is similar and consistent with the increased popularity of synthetic cannabinoids in Europe since 2008.

Synthetic cannabinoids are being encountered in most regions of the United States with the substances found as adulterants on plant material or being abused alone as self-reported on internet discussion boards.

Data gathered from published studies, supplemented by internet discussion websites, and personal communications demonstrate that these products are being abused mainly by smoking for their psychoactive properties and are marketed as “legal” alternatives to marijuana. This characterization and their reputation as potent herbal intoxicants increased their popularity. These substances alone or laced on plant material have the potential to be extremely harmful due to their method of manufacture and the potency of the substances. Smoking mixtures of these substances for the purpose of achieving intoxication has resulted in numerous emergency room visits and calls to poison control centers. Numerous states, local jurisdictions, and the international community have also controlled these substances.

Youth appear to be the primary abusers of synthetic cannabinoids and synthetic cannabinoid-containing products, as supported by law enforcement encounters and reports from emergency rooms; however, all age groups have been discussed in media reports as abusing these substances and related products. More recently, clandestinely produced synthetic cannabinoid products have been encountered in liquid forms, and law enforcement has communicated that these designer drug products are intended for use in electronic cigarettes and vaporizers.

5. *The Scope, Duration, and Significance of Abuse:* As stated by the HHS, based on their pharmacological properties, it is reasonable to assume that, if uncontrolled, the scope, duration, and significance of UR-144, XLR11, and AKB48 abuse could be similar to marijuana. National

Forensic Laboratory Information Systems (NFLIS),³ a national database capturing data from forensic laboratories, has reported 46,324 reports (January 2010 to December 2014) related to UR-144, XLR11, and AKB48 from 44 states (query date: April 30, 2015). From January 1, 2010, through December 31, 2014, according to the System to Retrieve Information on Drug Evidence (STRIDE) and STARLiMS data,⁴ there were 2,049 reports involving 245 cases for UR-144, 4,041 reports involving 487 cases for XLR11, and 201 reports involving 63 cases for AKB48 (query date: April 30, 2015). Recently, numerous exposure incidents have been documented by poison control centers in the United States as the abuse of synthetic cannabinoids has become associated with both acute and long-term public health and safety concerns. The American Association of Poison Control Centers (AAPCC) has reported exposure calls corresponding to products purportedly laced with synthetic cannabinoids since 2011, although the data provided do not generally include biological sample testing that would confirm the specific cannabinoid. AAPCC reported 6,968 exposure calls in 2011 and 5,230 calls in 2012. While exposure calls decreased in 2013 to 2,668, calls involving exposure to a synthetic cannabinoid rebounded in 2014 reaching 3,680. In addition, 623 calls have been reported from January 1 through February 28, 2015. A majority of exposure incidents resulted in seeking medical attention at health care facilities. In 2010, the Substance Abuse and Mental Health Services Administration (SAMHSA) reported 11,406 emergency department visits involving a synthetic cannabinoid product. In 2011, SAMHSA reported the number of emergency department visits involving a synthetic cannabinoid product had increased 2.5 times to 28,531.

³ NFLIS is a program of the DEA that collects drug identification results from drug cases analyzed by other Federal, State, and local forensic laboratories.

⁴ STRIDE collected the results of drug evidence analyzed at DEA laboratories and reflects evidence submitted by the DEA, other Federal law enforcement agencies, and some local law enforcement agencies. On October 1, 2014, STARLiMS replaced STRIDE as the DEA laboratory drug evidence data system of record.

6. *What, if Any, Risk There is to the Public Health:* Law enforcement, military, and public health officials have reported exposure incidents that demonstrate the dangers associated with abuse of synthetic cannabinoids to both the individual abusers and those connected to the misuse and abuse of these substances not intended for human use. Warnings regarding the dangers associated with abuse of synthetic cannabinoids and their products have been issued by numerous state public health departments, poison control centers, and private organizations. Detailed product analyses describe large variations in the amount of synthetic cannabinoid laced on the plant material even within samplings of the same product. These unknowns present a significant risk of danger to the abusing individuals. Some of the common clinical effects reported in emergency rooms in response to the abuse of synthetic cannabinoids include: vomiting, anxiety, agitation, irritability, seizures, hallucinations, tachycardia, elevated blood pressure, and loss of consciousness.

At least one death has been reported in Minnesota following ingestion of UR-144 and XLR11. In 2013, in California, a 27-year-old female developed hypertension, tachycardia, and rhabdomyolysis prior to being intubated and admitted to the ICU for protection of the airway following ingestion of a synthetic cannabinoid product containing XLR11. A 33-year-old-man developed acute cerebral ischemia and infarction shortly following the use of XLR11. In addition, reports have detailed various driving under the influence cases where users operated a motor vehicle while intoxicated with synthetic cannabinoids, including UR-144, XLR11, and/or AKB48.

In February 2013, the Centers for Disease Control (CDC) reported on an association between XLR11 exposure and acute kidney injury. The CDC examined 16 patients with acute kidney injury who reported recent smoking of synthetic cannabinoids. Seven of the 16 patients smoked

substances that were positive for XLR11 or its metabolite. In addition, one of these seven cases also tested positive for UR-144.

Additional cases reported adverse health effects including nausea, vomiting, agitation, panic attacks, involuntary muscle twitching and confusion following ingestion of UR-144 and/or XLR11.

7. Its Psychic or Physiological Dependence Liability: Chronic abuse of synthetic cannabinoids has been linked to signs of addiction and withdrawal. According to the HHS, the pharmacologic profiles of UR-144, XLR11, and AKB48 strongly suggest that they possess physiological and psychological dependence liability that is similar to that of delta-9-tetrahydrocannabinol (Δ^9 -THC) (schedule I) and JWH-018 (schedule I). Additionally, tolerance to these drugs may develop fairly rapidly with larger doses being required to achieve the desired effect. However, there are no studies or case reports that document the psychic or physiological dependence potential of UR-144, XLR11, or AKB48.

8. Whether the Substance is an Immediate Precursor of a Substance Already Controlled Under the CSA: UR-144, XLR11, and AKB48 are not considered immediate precursors of any controlled substance of the CSA as defined by 21 U.S.C 802(23).

Conclusion: Based on consideration of the scientific and medical evaluations and accompanying recommendation of the HHS, and based on the DEA's considerations of its own eight-factor analysis, the DEA finds that these facts and all other relevant data constitute substantial evidence of the potential for abuse of UR-144, XLR11, and AKB48. As such, the DEA hereby proposes to schedule UR-144, XLR11, and AKB48 as controlled substances under the CSA.

Proposed Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as schedules I, II, III, IV, and V. The CSA also outlines the findings required to place a drug or other substance in any particular schedule. 21 U.S.C. 812(b). After consideration of the analysis and recommendation of the Assistant Secretary for HHS and review of all other available data, the Administrator of the DEA, pursuant to 21 U.S.C. 811(a) and 21 U.S.C. 812(b)(1), finds that:

- (1) (1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (UR-144), [1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144, XLR11), and *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48) have a high potential for abuse that is comparable to other schedule I substances such as delta-9-tetrahydrocannabinol (Δ^9 -THC) and JWH-018;
- (2) (1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (UR-144), [1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144, XLR11), and *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48) have no currently accepted medical use in treatment in the United States; and
- (3) There is a lack of accepted safety for use of (1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (UR-144), [1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144, XLR11) and *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48) under medical supervision.

Based on these findings, the Administrator of the DEA concludes that (1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (UR-144), [1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144, XLR11), and *N*-(1-

adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48) including their salts, isomers and salts of isomers, whenever the existence of such salts, isomers, and salts of isomers is possible, warrant control in schedule I of the CSA. 21 U.S.C. 812(b)(1).

Requirements for Handling UR-144, XLR11 and AKB48

If this rule is finalized as proposed, persons who handle UR-144, XLR11, or AKB48 would continue⁵ to be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, possession, importing, and exporting of schedule I controlled substances, including those listed below:

1. *Registration.* Any person who handles (manufactures, distributes, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses) UR-144, XLR11, or AKB48, or who desires to handle UR-144, XLR11, or AKB48 would be required to be registered with the DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Security.* UR-144, XLR11, and AKB48 would be subject to schedule I security requirements and would need to be handled and stored pursuant to 21 U.S.C. 821, 823, and 871(b), and in accordance with 21 CFR 1301.71–1301.93.

3. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of UR-144, XLR11, and AKB48 would need to be in compliance with 21 U.S.C. 825 and 958(e), and be in accordance with 21 CFR part 1302.

4. *Quota.* Only registered manufacturers would be permitted to manufacture UR-144, XLR11, or AKB48 in accordance with a quota assigned pursuant to 21 U.S.C. 826 and in accordance with 21 CFR part 1303.

⁵ UR-144, XLR11, and AKB48 are currently subject to schedule I controls on a temporary basis, pursuant to 21 U.S.C. 811(h).

5. *Inventory.* Every DEA registrant who possesses any quantity of UR-144, XLR11, and/or AKB48 on the effective date of the final rule would be required to continue to maintain an inventory of all stocks of UR-144, XLR11, and/or AKB48 on hand, pursuant to 21 U.S.C. 827, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

6. *Records and Reports.* Every DEA registrant would be required to maintain records and submit reports with respect to UR-144, XLR11, and/or AKB48 pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR parts 1304 and 1312.

7. *Order Forms.* Every DEA registrant who distributes UR-144, XLR11, and/or AKB48 would be required to comply with the order form requirements, pursuant to 21 U.S.C. 828, and 21 CFR part 1305.

8. *Importation and Exportation.* All importation and exportation of UR-144, XLR11, and AKB48 would need to be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

9. *Liability.* Any activity involving UR-144, XLR11, or AKB48 not authorized by, or in violation of the CSA or its implementing regulations would be unlawful, and could subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Executive Orders 12866 and 13563

In accordance with 21 U.S.C. 811(a), this proposed scheduling action is subject to formal rulemaking procedures done “on the record after opportunity for a hearing,” which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of

Management and Budget (OMB) pursuant to Section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988

This proposed regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132

This proposed rulemaking does not have federalism implications warranting the application of Executive Order 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175

This proposed rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act (RFA), 5 U.S.C. 601-602, has reviewed this proposed rule and by approving it certifies that it will not have a significant economic impact on a substantial number of small entities. On May 16, 2013, the Deputy Administrator published a Final Order in the Federal Register (78 FR 28735) amending 21 CFR 1308.11(h) to temporarily place these three synthetic cannabinoids into schedule I of the

CSA pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). All entities that currently handle or plan to handle these synthetic cannabinoids are estimated to have already established and implemented the systems and processes required to handle UR-144, XLR11, and AKB48. Therefore, the DEA anticipates that this proposed rule will impose minimal or no economic impact on businesses that currently handle UR-144, XLR11, or AKB48 for lawful purposes. This estimate applies to entities large and small. Therefore, DEA has concluded that this proposed rule will not have a significant effect on a substantial number of small entities.

Unfunded Mandates Reform Act of 1995

On the basis of information contained in the “Regulatory Flexibility Act” section above, the DEA has determined and certifies pursuant to the Unfunded Mandates Reform Act (UMRA) of 1995 (2 U.S.C. 1501 *et seq.*), that this action would not result in any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted for inflation) in any one year. Therefore, neither a Small Government Agency Plan nor any other action is required under provisions of the UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR part 1308 is proposed to be amended to read as follows:

PART 1308— SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for 21 CFR part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

2. Amend § 1308.11 by:

- a. Adding paragraphs (g)(16) through (18); and

- b. Removing paragraphs (h)(1) through (3) and redesignating paragraphs (h)(4) through (23) as paragraphs (h)(1) through (20), respectively.

The additions read as follows:

§ 1308.11 Schedule I.

* * * * *

(g) * * *

(16) (1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (UR-144).....(7144)

(17) [1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144, XLR11).....(7011)

(18) *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48).....(7048)

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Dated: May 12, 2015.

Michele M. Leonhart,
Administrator.

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